**REMARKS**

Claims 1, 2, 4-10 and 12-14 are pending in the instant application. Claims 1, 2, 4-10 and 12-14 have been rejected. Claim 1 has been amended. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

**I. Election/Restriction**

The Restriction Requirement wherein Applicants elected a 3'-untranslated region of a nucleic acid molecule encoding macrophage inflammatory protein-3 alpha (SEQ ID NO: 3) has been proper and made Final. Accordingly, Applicants have amended claim 1 to remove reference to other regions of this sequence, reserving the right to file a continuing application on the canceled subject matter.

**II. Rejection of Claims Under 35 U.S.C. 103(a)**

The rejection of claims 1, 2, 4-10 and 12-14 under 35 U.S.C. 103(a) as being unpatentable over Schlegel et al. (WO 01/42467) and Hromas (US Patent 6,096,300), and further in view of Baracchini et al. (US Patent 5,801,154) and Fritz et al. (1997)

has been maintained for reasons of record. The Examiner suggests it would have been *prima facie* obvious for one of ordinary skill to target and inhibit expression of macrophage inflammatory protein 3-alpha because the prior art has taught antisense oligonucleotides complementary to this gene can inhibit expression of the gene (Schlegel et al. and Hromas), while one of skill would have been motivated by the teaching in the art of the critical role for this gene in regulation of mononuclear chemotaxis (Hromas). The Examiner suggests one of skill would have had an expectation of success based on the teachings of the cited references. Finally, the motivation to modify antisense is provided for by the teaching of Baracchini et al. and Fritz et al. The Examiner also suggests that Baracchini et al. teach targeting the 3'-untranslated region of a gene with antisense while Hromas discloses the sequence of this region. Applicants respectfully traverse this rejection.

At the outset, Applicants have amended the claims to recite a specific nucleobase region within the sequence of macrophage inflammatory protein 3-alpha for targeting of antisense compounds, a region that is not taught or suggested in the cited references. Support for this amendment can be found throughout

the specification as filed but in particular at pages 104-105, Table 1, where it is clearly shown that antisense compound targeted to the cited region, nucleobases 361 through 425, have significant activity to inhibit expression of the gene.

Schlegel et al. disclose and claim an isolated nucleic acid molecule which is at least 90% homologous to human macrophage inflammatory protein 3-alpha or a fragment or complement thereof, which can hybridize under conditions of moderate or high stringency, as well as use of an antisense oligonucleotide complementary to a polynucleotide corresponding to this gene for treatment of cervical cancer. Nowhere does this patent, either alone or when combined with other cited references, teach or suggest antisense compounds as now claimed which are targeted to a specific nucleobase region within the sequence of SEQ ID NO: 3.

Hromas discloses and claims the human macrophage inflammatory protein 3-alpha DNA and protein sequence. Also disclosed is the use of antisense polynucleotides to this gene in general. No specific antisense compounds are taught or suggested, nor is any nucleobase region within the sequence of this gene that could be successfully targeted with antisense. Therefore, either alone or when combined with other cited

references, this reference fails to teach or suggest the invention of the amended claims.

The secondary references cited fail to overcome the deficiencies in teaching of these primary references.

The '154 patent teaches modification to antisense oligonucleotides in general as a way to enhance activity. However, this general discussion of modified oligonucleotides does not teach or suggest use of antisense compounds of any type to target macrophage inflammatory protein 3-alpha and the successful inhibition of expression using antisense.

Fritz et al. (1997) disclose cationic polystyrene nanoparticles as carrier systems for antisense compounds in general. This paper, however, does not teach or suggest use of antisense compounds of any type to target the human macrophage inflammatory protein 3-alpha, and the successful inhibition of expression using antisense.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference

teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. The limitations of the claims as now amended, which specify a specific nucleobase region within the sequence of human macrophage inflammatory protein 3-alpha that can be successfully targeted with antisense and result in inhibition of the expression of the gene, is not taught or suggested by any of the references individually or when combined. Therefore, the limitations of the claims as amended clearly are not taught or suggested by the combination of prior art references, nor is any expectation of successful use of such antisense compounds provided by the combination of prior art. It is only with the specification in hand that one of skill would understand that this specific region of the gene could be successfully targeted with antisense compounds and result in inhibition of gene expression. Thus, the combination of prior art cited cannot render the instant claimed invention obvious. Withdrawal of this rejection is therefore respectfully requested.

**III. Conclusion**

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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